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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/518,966	11/04/2005	Jolanta Gutkowska	29105/40749	8084

4743 7590 07/14/2008

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EXAMINER	
NIEBAUER, RONALD T	
ART UNIT	PAPER NUMBER
1654	
MAIL DATE	DELIVERY MODE
07/14/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/518,966	GUTKOWSKA ET AL.	
	Examiner	Art Unit	
	RONALD T. NIEBAUER	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) *5,6,17,18,31 and 32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7-16,19-30 and 33-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 December 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/25/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group 1 (claims 3 in part,4,15 in part,16,29 in part, 30) and the following species

oxycotin or functional derivative: SEQ ID NO:1

non-cardiomyocyte type: embryonic stem cell

phenotypic feature: level of ion channels

disease: heart infarction

in the reply filed on 3/27/08 is acknowledged.

Claims 5-6,17-18,31-32 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 3/27/08. In particular, claims 5-6,17-18,31-32 are part of Group 4, not elected Group 1.

Claims 42-69 have been cancelled.

Claims 1-4,7-16,19-30,33-41 are under consideration.

In the course of searching for the elected species any art that was uncovered that reads on non-elected species is cited herein.

Specification

The disclosure is objected to because of the following informalities:

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. In particular, page 24 line 24 of the specification includes an embedded hyperlink.

Appropriate correction is required.

Claim Objections

Applicant is advised that should claim 7/19/33 be found allowable, claims 9/20/35 respectively will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). In the instant case claims 7/19/33 recite that the non-cardiomyocyte is a stem or progenitor cell. Claims 9/20/35 recite that the stem or progenitor cell is selected from the group consisting of circulating and non-circulating stem or progenitor cells. However, reciting circulating or non-circulating does not limit the claim since there are no other possibilities. In other words claims 7/19/33 and claims 9/20/35 respectively cover the same scope.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3,15,29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3,15, and 29 recite 'oxytocin or a functional derivative thereof'. The specification (page 15 last paragraph – page 16) states that a functional derivative possesses activity that is substantially similar to the activity of the whole protein sequence and includes, for example, fragments, segments, variants, and analogs. Analogs and variants are further defined (page 16-17). However, the term 'functional derivative' renders the claims indefinite. The term functional derivative' is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Although applicant provides a definition of the claim, the definition itself does not clearly set forth the metes and bounds of the claim. For example, a standard for ascertaining activity that is substantially similar has not been set forth. Further, the term 'variant' is stated to mean a protein that is substantially similar in structure. However, a standard for ascertaining structure that is substantially similar has not been set forth.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1-3,7-15,19-29,33-41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the

relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus …") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. The MPEP does state that for a

generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163. While all of the factors have been considered, a sufficient amount for a *prima facie* case are discussed below.

In the instant case, claims 1,7-13,19-27,33-41 are drawn to a methods of inducing differentiation or treating a disease that comprise stimulating oxytocin receptor or inducing differentiation. Claims 1,7-13,19-27,33-41 are not limited to any particular structure. Claims 2,14,28 refer to the use of agents. Claims 3,15,29 recite particular agents and functional derivatives of oxytocin. Although unclear (see 112 2nd) for purposes of examination the term 'functional derivative' has been given the broadest reasonable interpretation such that any agent with at least any similarity of structure or function is a functional derivative.

(1) Level of skill and knowledge in the art:

The level of skill in the art is high.

(2) Partial structure:

Claims 1,7-13,19-27,33-41 are drawn to methods of inducing differentiation or treating a disease that comprise stimulating oxytocin receptor or inducing differentiation. Claims 1,7-13,19-27,33-41 are not limited to any particular structure. Claims 2,14,28 refer to the use of agents. Claims 3,15,29 recite particular agents and functional derivatives of oxytocin. However, the claims are not limited to any particular recited structure. Although unclear (see 112 2nd) for purposes of examination the term 'functional derivative' has been given the broadest reasonable interpretation. In considering the possible variability, many different structures are possible. In simply considering functional derivatives if any 5 amino acids of oxytocin were substituted to any of the 20 natural amino acids there would be over 3 million different possible structures. Hence, there is substantial variability in the genus.

The specification (claim 3) refers to oxytocin, retinoic acid and T3. The specification provides specific examples of oxytocin and a limited subset of functional derivatives recited in claim 4 for example (which is not rejected for lack of written description). No other specific examples of segments, variants, analogs, or chemical derivatives has been provided. Since there are a substantial variety of polypeptides possible within the genus, the examples do not constitute a representative number of species and do not sufficiently describe the genus claimed (see Gostelli above).

(3) Physical and/or chemical properties and (4) Functional characteristics:

Claims 1 and 13 recite that OTR activity is stimulated. Claims 1 and 24 recite that differentiation is induced. Claims 2,14,and 28 expressly state that the agents are capable of stimulating OTR activity. However, there is no disclosed correlation between structure and function. There are no common attributes or characteristics that identify agents effective to induce differentiation or agents to stimulate OTR activity. In particular, no common core sequence is taught. Regarding the functional derivatives, there is no teaching in the specification regarding what part of the structure can be varied while retaining the ability to induce differentiation or stimulate OTR activity. Such teaching is relevant since structure is not necessarily a reliable indicator of function. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus and that there is a lack of the knowledge in the art regarding which amino acids can vary to maintain the function and thus that the applicant was not in possession of the claimed genus.

(5) Method of making the claimed invention:

The specification (page 39 line 20) refers to the use of OT and retinoic acid (page 47 line 32), however the specification fail to describe the use of a representative number of other agents, segments, variants, analogs, or chemical derivatives.

As stated *supra*, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that the claims is/are broad and generic, with respect to all possible agents and functional derivatives encompassed by the claims. The possible structural variations are many. Although the claims may recite some functional characteristics, the claims lack written description because there is no

disclosure of a correlation between function and structure of the agents beyond those agents specifically disclosed in the examples in the specification. Moreover, the specification lacks sufficient variety of species to reflect this variance in the genus. While having written description of agents identified in the specification tables and/or examples, the specification does not provide sufficient descriptive support for the myriad of agents embraced by the claims.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-3,7,9-15,19-21,23-25,27-29,33,35,38-39,41 are rejected under 35 U.S.C. 102(b) as being anticipated by Umezawa et al. (WO 01/48149 as cited in the IDS).

Claims 1-3,7,9-15,19-21,23-25,27-29,33,35,38-39,41 are rejected under 35 U.S.C. 102(e) as being anticipated by Umezawa et al. (US 2002/0142457).

WO 01/48149, which is not in the English language, is from PCT/JP00/01148. US 2002/0142457, which is in the English language, is a CON of PCT/JP00/01148. Since US 2002/0142457 is in the English language all references below will be to US 2002/0142457.

Umezawa teach methods of differentiation of cells having the potential to differentiate into cardiomyocytes (abstract, claims 52,91). Umezawa teach therapeutic agents for various heart diseases containing cells having the potential to differentiate into cardiomyoctes (abstract). Umezawa teach that cardiomyocytes can be differentiated from embryonic stem cells (section 0006, claim 3). Umezawa teach a transplantation experiment in which cells were transplanted into an adult mouse heart and the cells were differentiated into myocardia (section 0013). Umezawa teach humans and animals as the donor for the cells (section 0112, 0114, claim 24). Umezawa teach the use of factors to induce differentiation of cells (section 0132) specifically vitamins (section 0135) particularly retinoic acid (section 0141, 0163, claim 34, 57,72, section 0449 example 16). Umezawa teach heart diseases such as myocardial infarction and heart failure as targets of the therapeutic agents (section 0152). Umezawa teach transportation of the agents (section 0157) or cells (claim 40). Umezawa teach techniques in which cells are used from the patient of interest (section 0235). Umezawa teach method for regenerating heart damage (claim 76). Umezawa teach methods of obtaining stem cells from mice (section 0321 and example 1).

Umezawa teach the addition of retinoic acid to the stem cells to stimulate cardiomyoctye differentiation (section 0337 and example 3). Umezawa teach transplantation of cells into mice (section 0389 and example 8).

Since Umezawa teach contacting stem cells in vitro with retinoic acid (section 0337 and example 3, section 0360 example 5, section 0449 and example 16) the limitations of claims 1-3,7,9-10,12 of the instant invention are met (see discussion about claim 1,9 and 12 below).

Umezawa teach therapeutic agents for various heart diseases containing cells having the potential to differentiate into cardiomyoctes (abstract). Umezawa teach heart diseases such as myocardial infarction (i.e. heart infarction, the elected species of disease) and heart failure as targets of the therapeutic agents (section 0152). In example 5, Umezawa teach the addition of retinoic acid to mouse bone marrow derived stem cells (section 0349,0360). In example 8, Umezawa teach the transplantation (i.e. in vivo) of the treated mouse bone marrow derived stem cells into a mouse (section 0389-0390) (i.e. allogenic from mouse to mouse) and the mouse bone marrow cell differentiated into cardiomyocytes (section 0394). As such, the limitations of claims 11,13-15,19-21,23-25,27-29,33,35,38-39,41 of the instant invention are met (see discussion about claims 13,20,35,41 below).

It is noted that claims 1,13 recite stimulation of OTR activity. Since Umezawa teach the use of retinoic acid, which as claimed (claim 3) is an agent to stimulate OTR activity, the claim limitations are necessarily met.

As discussed above (claim objections) claim 9,20,35 are duplicate claims. It is noted that the stem cells were derived from mouse bone marrow (section 0322,0336).

It is noted that claims 12,41 recites features of the cardiomyocyte. Although Umezawa does not report features of all the cardiomyoctes such as those obtained after retinoic acid addition, Umezawa does report that the cardiomyocyte cells were beating (section 0349). Please note, since the Office does not have the facilities for examining and comparing Applicants' composition (i.e. cells) with the composition (i.e. cells) of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed cells and the cells of the prior art. *See In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980), and "as a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972).

Although unclear (see 112 2nd) for purposes of examination the term 'functional derivative' has been given the broadest reasonable interpretation such that any agent with at least any similarity of structure or function is a functional derivative.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3,7-15,19-29,33-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Umezawa et al. (WO 01/48149 as cited in the IDS) or Umezawa et al. (US 2002/0142457).

WO 01/48149, which is not in the English language, is from PCT/JP00/01148. US 2002/0142457, which is in the English language, is a CON of PCT/JP00/01148. Since US 2002/0142457 is in the English language all references below will be to US 2002/0142457.

As discussed above Umezawa teach claims 1-3,7,9-15,19-21,23-25,27-29,33,35,38-39,41 of the instant invention.

Umezawa does not expressly teach in a single embodiment the use of embryonic stem cells (see claims 8,34 of the instant invention), the use in humans (compare claims 22,26 of the instant invention), autologous use (compare claims 36-37 of the instant invention), and xenogenic use (compare claim 40 of the instant invention).

Umezawa does teach that cardiomyocytes can be differentiated from embryonic stem cells (section 0004, 0006, claim 3). As such, one would be motivated to substitute embryonic stem cells for the bone marrow derived stem cells that are used in the examples (section

0349,0360, example 3). Thus, the elected species of cell type and the limitations of claims 8,34 are met.

Umezawa does teach humans and animals as the donor for the cells (section 0112, 0114, claim 24). As such, one would be motivated to substitute humans for the mice that are used in the examples (example 5,8) thus meeting the limitations of claims 22,26 of the instant invention.

Umezawa teach the transplantation (i.e. in vivo) of the treated mouse bone marrow derived stem cells into a mouse (section 0389-0390) (i.e. allogenic from mouse to mouse) and the mouse bone marrow cell differentiated into cardiomyocytes (section 0394). To avoid the possibility of rejection one would be motivated to use cells from the same source thus meeting the limitations of claims 36-37 of the instant invention. Further, since Umezawa teach both humans and animals as the donor for the cells (section 0112, 0114, claim 24) one would be motivated to try the use of particular cells in different species thus meeting the limitation of claim 40 of the instant invention, for example, in order to optimize the ease of use, cost, etc.

Exemplary rationales in supporting a 103 rejection include the simple substitution of one known element for another to obtain a predictable result (KSR v. Teleflex and MPEP section 2141 III).

Furthermore, The KSR court concluded that "obvious to try" may be an appropriate test under 103. The Supreme Court stated in *KSR*

> When there is motivation
>
> > "to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103." *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, ___, 82 USPQ2d 1385, 1397 (2007).

In the instant case, the claims would have been obvious because the substitution of one known element for another would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Further, since Umezawa as discussed above teach a finite number of cell types (bone marrow stem cells and embryonic stem cells for example), administrations (in vitro and in vivo), and donor cells (mice, humans for example) the claims would have been obvious because a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. Further, Umezawa recognized the problem of differentiating cells into cardiomyocytes (abstract). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Although unclear (see 112 2nd) for purposes of examination the term 'functional derivative' has been given the broadest reasonable interpretation such that any agent with at least any similarity of structure or function is a functional derivative.

Claims 1-4,7-16,19-30,33-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Umezawa et al. (WO 01/48149 as cited in the IDS) or Umezawa et al. (US 2002/0142457) and Uvnas-Moberg et al. (WO 00/18424), Gutkowska et al. (PNAS v94 1997 pages 11704-11709) and Sapino et al. (Endocrinology v133 1993 pages 838-842).

WO 01/48149, which is not in the English language, is from PCT/JP00/01148. US 2002/0142457, which is in the English language, is a CON of PCT/JP00/01148. Since US 2002/0142457 is in the English language all references below will be to US 2002/0142457.

As discussed above Umezawa render obvious claims 1-3,7-15,19-29,33-41of the instant invention.

Umezawa does not teach oxytocin or oxytocin derivative of the structure shown in claims 4,16,30 of the instant invention.

Umezawa does teach therapeutic agents for heart diseases (abtract). Umezawa teach a range of myocardium-forming agents (section 0159, claims 67-69) including various amino acid sequences (claim 70).

Uvnas-Moberg et al. (WO 00/18424) teach that substances with oxytocin activity improve cell regeneration (abstract). Uvnas-Moberg teach oxytocin (page 1 line 15) which is identical to the elected species of oxytocin as in claims 4,16,30 of the instant invention. Uvnas-Moberg teach that oxytocin is suggested to participate in the control of cardiovascular functions (page l lines 23-24) and teach oxytocin injections (page l lines 26 - page 2 line 3; claim 8) to be used for administrations for conditions such as heart infarction.

Sapino et al. (Endocrinology v133 1993 pages 838-842) teach that oxytocin exerts a trophic effect on myoepithelial cells and enhances cell differentiation (abstract).

Gutkowska et al. (PNAS v94 1997 pages 11704-11709) teach that oxytocin interacts with oxytocin receptors in the heart and releases ANP (abstract, title).

Taken together since Umezawa teach a variety of myocardium-forming agents one would be motivated to try specific agents taught in the prior art. Uvnas-Moberg teach the importance of oxytocin specifically in relation to heart infarction, the same patient population taught by Umezawa. Further, Gutkowska also point to the role of oxytocin and its function in the heart. Sapino show that oxytocin enhances cell differentiation in myoepithelial cells. Since oxytocin enhances cell differentiation in myoepithelial cells one would be motivated to use oxytocin in other types of cells such as embryonic stem cells as taught by Umezawa.

Exemplary rationales in supporting a 103 rejection include the simple substitution of one known element for another to obtain a predictable result (KSR v. Teleflex and MPEP section 2141 III).

Furthermore, the KSR court concluded that "obvious to try" may be an appropriate test under 103. The Supreme Court stated in *KSR*

> When there is motivation
>
> > "to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103." *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, ___, 82 USPQ2d 1385, 1397 (2007).

In the instant case, the claims would have been obvious because the substitution of one known element (oxytocin as an agent for cell differentiation, see Sapino above) for another (retinoic acid as an agent for cell differentiation as taught by Umezawa) would have yielded predictable results to one of ordinary skill in the art at the time of the invention. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. In particular, Sapino teach

that oxytocin exerts a trophic effect on myoepithelial cells and enhances cell differentiation and Uvnas-Moberg teach oxytocin injections (page l lines 26 - page 2 line 3) to be used for administrations for conditions such as heart infarction. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Although unclear (see 112 2nd) for purposes of examination the term 'functional derivative' has been given the broadest reasonable interpretation such that any agent with at least any similarity of structure or function is a functional derivative.

Relevant Prior art

The prior art that remains of record and not relied upon is considered pertinent to applicant's disclosure: Rodriguez et al. (as cited in IDS and in restriction requirement) remains of record. Rodriguez et al. teach a method of inducing cardiac differentiation in P19 cells by treating them with triiodo-L-thryronine (abstract). Any rejection using Rodriguez would be duplicative of rejections recited above.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to RONALD T. NIEBAUER whose telephone number is (571)270-3059. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, alt. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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